

Attorney Docket No.: 960296.95360
Applicant: Ronald T. Raines
Application No.: 09/234,028 Filed: 01/20/1999
Group Art Unit: 1652
Examiner: Richard G. Hutson
Reply to Office Action dated: September 24, 2007
Response dated: October 31, 2007

AMENDMENT TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1. (Currently amended) An oxidation-resistant engineered ribonuclease inhibitor (RI) variant selected from the group consisting of

(i) an native RI variant differing from reference SEQ ID NO: 3, which has wherein the difference consists of at least one pair of adjacent cysteine of the residues [[,]] at positions 95, 96, 329 and 330 being an alanine; and

(ii) an RI variant differing from reference SEQ ID NO: 2, wherein the difference consists of at least one of the residues at positions 324 and 325 being an alanine,

the variant differing from the native RI by a substitution in at least one cysteine of the at least one pair of adjacent cysteine residues in the native RI amino acid sequence, the amino acid residue substituting for the cysteine residue not capable of forming a disulfide bond with an adjacent residue, the substituted RI variant having a greater resistance to oxidation relative to the native RI, the substituted RI variant reference sequence for the variant and retaining its specificity and binding affinity to ribonuclease, wherein the native RI is defined as SEQ ID NO: 2 or SEQ ID NO: 3.

2. (Cancelled)

3. (Cancelled)

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4. (Currently amended) The ribonuclease inhibitor variant of claim 1, wherein the ~~substitution in at least one of the cysteine residues~~ difference inhibits the formation of a disulfide bond with an adjacent cysteine residue.

5. (Currently amended) The ribonuclease inhibitor variant of claim ~~1~~ 18, wherein the mutant variant ~~ribonuclease inhibitor~~ is 10 to 15 fold more resistant to oxidative damage than ~~[[the]]~~ a native ~~human~~ ribonuclease inhibitor.

6. (Cancelled)

7. (Currently amended) The ribonuclease inhibitor variant of claim 1, wherein the ~~modified ribonuclease inhibitor~~ variant exhibits an *in vitro* inhibition of ribonucleolytic activity.

8. (Cancelled)

9. (Currently amended) ~~A human~~ The ribonuclease inhibitor variant of claim 18, having ~~at least one amino acid substitution in at least one of two adjacent cysteine residues present in the amino acid sequence of the wild type ribonuclease inhibitor (SEQ ID NO:3), the substitution being an amino acid other than cysteine not capable of forming a disulfide bond with an adjacent amino acid residue, the remainder of the variant having the amino acid sequence of the wild type ribonuclease inhibitor, the substituted ribonuclease inhibitor having a greater resistance to oxidation, the substituted ribonuclease inhibitor retaining the specificity and binding affinity for binding to angiogenin of the RI wild type human ribonuclease inhibitor reference~~ SEQ ID NO:3.

10. -17. (Cancelled)

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18. (new) An oxidation-resistant ribonuclease inhibitor (RI) variant differing from reference SEQ ID NO: 3, wherein the difference consists of at least one of the residues at positions 95, 96, 329 and 330 being an alanine.

19. (new) An RI variant of Claim 18, the residues at positions 329 and 330 being alanine residues.

20. (new) An oxidation-resistant ribonuclease inhibitor (RI) variant differing from reference SEQ ID NO: 2, the difference consisting of at least one of the residues at positions 324 and 325 being an alanine.